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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Cao et al	§	**ART UNIT: 1635**
FILED: August 3, 2000	§	
SERIAL NO.: 09/631,411	§	**EXAMINER: Lacourciere, K.**
FOR: Interaction of Smad6 with Hox Proteins and Uses Thereof	§	**DOCKET: D6258**

MS Appeal Brief - Patents
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313

TRANSMITTAL OF APPEAL BRIEF
AND CERTIFICATE OF MAILING UNDER 37 CFR 1.8

Dear Sir:

Enclosed please find three originals of the Appeal Brief for the above-referenced patent application.

The Commissioner is hereby authorized to charge Deposit Account No. 07-1185 in the total amount of $165 for the appeal fee and any additional fee that may be required. Please credit any overpayment or debit any underpayment to Deposit Account 07-1185.

I hereby certify under 37 CFR 1.8 that the following correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to MS Appeal Brief, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. Please return the enclosed postcard acknowledging receipt of this correspondence.

Respectfully submitted,

Date: Nov 18, 2003

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713)-270-5391
BADLER1@houston.rr.com

Benjamin Aaron Adler, Ph.D., J.D.
Counsel for Applicant
Registration No. 35,423

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P.O. Box 1450
Alexandria, VA 22313

ATTENTION: Board of Patent Appeals and Interferences

APPELLANT'S BRIEF

This Brief is in furtherance of the Notice of Appeal filed in this case on October 1, 2003. The fees required under 37 C.F.R. §1.17(f) and any other required fees are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

In accordance with 37 C.F.R. §1.192(a), this Brief is submitted in triplicate.

INDEX OF SUBJECT MATTER

I. REAL PARTY IN INTEREST

The real party in interest is the UAB Research Foundation.

II. RELATED APPEALS AND INTERFERENCES

Appellant is aware of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Originally claims 1-20 were filed with this Application. Claims 1-10 and 15-20 were withdrawn from consideration. The pending claims 11-14 are being appealed of which claim 11 is an independent claim.

IV. STATUS OF AMENDMENTS

No claim amendment was filed subsequent to the final rejection mailed June 3, 2003. All pending claims are shown in Appendix A.

V. SUMMARY OF THE INVENTION

The present invention shows that Smad6 interacts with Hoxc-8 as a transcriptional corepressor and inhibit transcriptional signaling in the nucleus (page 13, lines 3-13). The interaction between Smad6 and Hoxc-8 was identified by a yeast two-hybrid approach (page 22, lines 1-7; page 23, lines 5-7), and further demonstrated by co-immunoprecipitation assays in cells. Gel shift assays showed that Hoxc-8 interacted with Smad6 as a heterodimer when binding to DNA (page 25, lines 16-21). More importantly, the Smad6/Hoxc-8 complex inhibited both Smad1 interaction with Hoxc-8 in gel shift assays and transcription activity mediated by Smad1 (page 27, lines 5-19; page 28, lines 11-20). These results indicate that Smad6 functions as a transcriptional corepressor in

BMP signaling in the nucleus. Accordingly, the present invention provides a method of screening for drugs that may disrupt transcriptional repression by inhibiting the function of the Smad6/Hox complex (page 16, line 9 to page 17, line 2).

VI. ISSUES

Objection To Specification

Whether there is improper incorporation of subject matter in this application.

Rejection Under 35 U.S.C. §112

Whether claims 11-14 satisfy written description under 35 U.S.C. §112, first paragraph.

Whether claims 11-14 are indefinite under 35 U.S.C. §112, second paragraph.

VII. GROUPING OF CLAIMS

The rejected claims stand or fall together.

VIII. ARGUMENTS

Objection To Specification

The Examiner contends that the structure and physical activities of the proteins Smad6 and Hoxc-8 are essential to practice the claimed invention, and it is improper to incorporate essential material by reference to non-patent publications. Applicant respectfully disagrees.

Applicant submits that the practice of the present invention does not require knowledge about the structural features of Smad6 and Hoxc-8. The present invention only requires cloning and expressing Smad6 and Hoxc-8 in suitable vectors. Smad6 and Hoxc-8 are well known in the art. One of ordinary skill in the art can readily identify and obtain sequences for these proteins and clone these proteins according to standard genetic engineering procedures.

Hence, Applicant submits that the essential feature of the present invention is the identities of the proteins used (i.e. Smad6 and Hoxc-8), which is well known in the art. The structure and physical activities of the proteins Smad6 and Hoxc-8 are not essential to practice the claimed invention. In view of the detailed

description on the function and activities of Smad6 and Hoxc-8 presented in the instant specification, one of ordinary skill in the art could readily clone and express Smad6 and Hoxc-8 to practice the present invention. Accordingly, Applicant respectfully requests that this objection to the specification be reversed.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 11-14 stand rejected under 35 U.S.C. §112, first paragraph, for lack of possession of the claimed invention. Applicant respectfully requests that this rejection be reversed.

Applicant submits that the specification has provided sufficient written description for the claimed invention and possession of the invention has been shown by an actual reduction to practice. The specification has provided ample data on the interaction between Smad6 and Hoxc-8, demonstrating clearly that Applicant had possession of the claimed invention at the time the application was filed. The interaction between Smad6 and Hoxc-8 was identified in a yeast two-hybrid approach (Figure 1), and further demonstrated by co-immunoprecipitation assays in cells. Gel shift assays showed that Hoxc-8 interacted with Smad6 as a heterodimer when binding to DNA. More importantly, the Smad6/Hoxc-8

complex inhibited both Smad1 interaction with Hoxc-8 in gel shift assays and transcription activity mediated by Smad1 (Figures 3 and 4B).

The Examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. It is well established that the specification need only describe in detail material or procedure that is new or not conventional. The absence of definition or detail for well-established terms or procedures should not be the basis for a rejection under 35 U.S.C. §112, first paragraph, as lack of written description.

Applicant submits that Smad6 and Hoxc-8 proteins are well known in the art and one of ordinary skill in the art would readily recognize what these proteins are based on description disclosed herein. As described in the specification, Smads mediate signaling of the superfamily of transforming growth factor-β (TGF-β). Smad6 and Smad7, a subgroup of Smad proteins, antagonize

signaling of the well-known factor TGF-β. These two Smads, induced by TGF-β or bone morphogenetic protein, form stable association with activated type I receptors, which in turn block phosphorylation of ligand-induced Smads.

With regard to the Hox homeobox-containing transcription factor, there are 39 Hox homeobox-containing transcription factor genes in vertebrates. The genes, which are organized into four separate chromosome clusters, play critical roles in the process and patterning of vertebrate embryonic development. These 39 genes are subdivided into 13 paralogous groups on the basis of duplication of an ancestral homeobox cluster during evolution, sequence similarity and position within the cluster. Each paralog group has been demonstrated to be responsible for morphogenesis of a particular embryonic domain or structure. There are three members in Hox paralog group VIII: Hoxb-8, Hoxc-8 and Hoxd-8. Northern blot analysis shows that Hoxc-8 is expressed during human embryo development at high levels in spinal cord, backbone and limbs and at a lower level in heart.

In view of the above remarks, Applicant submits that one of ordinary skill in the art would readily recognize what Smad6 and

Hoxc-8 are. One of ordinary skill in the art is unlikely to be confused as to the identities of Smad6 and Hoxc-8.

Applicant submits that the specification has provided detailed description on the activities of Smad6 and Hoxc-8, and possession of the invention has been shown by an actual reduction to practice the claimed invention. Accordingly, Applicant respectfully requests that the rejection of claims 11-14 under 35 U.S.C. §112, first paragraph, be withdrawn.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 11-14 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicant respectfully requests that this rejection be reversed.

The Examiner contends that without structural information or description of physical characteristics for the Smad6 and Hoxc-8 proteins, one of ordinary skill in the art would not be able to discern what proteins are encompassed in the terms "Smad6" and "Hoxc-8". Applicant respectfully disagrees.

As discussed above, Smad6 and Hoxc-8 are well-known and extensively studied proteins in the art. In view of the level of skill and knowledge in the art, one of ordinary skill in the art would

readily recognize what Smad6 and Hoxc-8 proteins are. One of ordinary skill in the art is unlikely to be confused as to the identities of Smad6 and Hoxc-8. Indeed, the Examiner has not provided any evidence that a person having ordinary skill in this art would not readily recognize the identity of Smad6 and Hoxc-8.

Hence, Applicants submit that the Smad6 and Hoxc-8 proteins have been adequately described in the present application. The subject matter of claims 11-14 has been particularly pointed out and distinctly claimed. Accordingly, Applicant respectfully requests that the rejection of claims 11-14 under 35 U.S.C. §112, second paragraph, be withdrawn.

Respectfully submitted,

Date: Nov 13, 2003

Benjamin Aaron Adler, Ph. D., J.D.
Registration No. 35,423
Counsel for Applicant

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713) 270-5391
badler1@houston.rr.com

CLAIMS ON APPEAL

11. A method of screening for a compound that disrupts transcriptional repression of a gene, comprising the steps of:

(a) combining a Smad6/Hoxc-8 protein complex with a gene in the presence and absence of a compound, wherein said gene comprises a Hox DNA binding element; and

(b) assaying for transcription of said gene, wherein an increase in the level of transcription in the presence of said compound relative to the level of transcription in the absence of said compound is indicative of a compound that disrupts transcriptional repression of said gene.

12. The method of claim 11, wherein said transcription is assayed by means selected from the group consisting of a Northern blot, a Western blot, an enzymatic assay and a chemiluminescent assay.

13. The method of claim 11, wherein said gene is a reporter gene.

14. The method of claim 13, wherein said reporter gene is selected from the group consisting of β-galactosidase, luciferase, secreted alkaline phosphotase and CAT assay.

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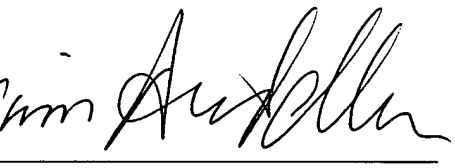

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